Amendments to the Claims

1-11. (cancelled)

12. (new) A method for the production of recombinant heterologous protein in prokaryotic cells comprising:

expressing a vector in said prokaryotic cells which comprises DNA encoding said heterologous protein operably linked to DNA encoding the OmpA signal peptide (SEQ ID NO:1);

wherein said DNA sequence encoding said OmpA signal peptide is operatively linked to a nucleic acid sequence encoding a peptide selected from the group consisting of SEGN (SEQ ID NO:2) and SEGNSD (SEQ ID NO:3); and

wherein said heterologous protein is secreted extracellularly as an active protein.

13. (new) The method according to claim 12, wherein said heterologous protein is secreted as a correctly folded protein.

14. (new) The method according to claim 12, wherein said nucleic acid sequence encodes the peptide SEGN (SEQ ID NO:2).

15. (new) The method according to claim 14, wherein said nucleic acid sequence comprises TCTGAGGGAAAC (SEQ ID NO:4).

16. (new) The method according to claim 12, wherein said nucleic acid sequence encodes the peptide SEGNSD (SEQ ID NO:3).

17. (new) The method according to claim 16, wherein said nucleic acid sequence comprises TCTGAGGGAAACAGTGAC (SEQ ID NO:5).

18. (new) The method according to claim 12, wherein the prokaryotic cell is *E. coli*.

19. (new) A method for the production of recombinant heterologous protein in prokaryotic cells comprising:

a) amplifying DNA encoding said heterologous protein by PCR;

b) purifying the PCR product;

c) inserting said PCR product into a vector,

wherein said vector comprises a DNA encoding an OmpA signal peptide, a peptide selected from the group consisting of SEGN (SEQ ID NO: 2) and SEGNSD (SEQ ID NO:3), and DNA encoding gpIII; and

wherein said PCR product is operably linked downstream to the DNA encoding the OmpA signal peptide and operably linked upstream to the DNA encoding gpIII of said vector;

d) inserting a stop codon between the heterologous protein and gpIII; and

e) expressing said vector in the prokaryotic cell.

20. (new) The method according to claim 19, further comprising:

f) purifying said heterologous protein.

21. (new) The method according to claim 12, wherein the heterologous protein is tissue plasminogen activator or a fragment thereof.

22. (new) The method according to claim 21, wherein the tissue plasminogen activator is human tissue plasminogen activator.

23. (new) The method according to claim 21, wherein said heterologous protein is a fragment selected from the group consisting of:

a) Finger domain (amino acids 4-50 of SEQ ID NO:18);

b) Growth factor domain (amino acids 50-87 of SEQ ID NO:18);

c) Kringle domain 1 (amino acids 86-176 of SEQ ID NO:18);

d) Kringle domain 2 (amino acids 176-262 of SEQ ID NO:18); and

e) Protease domain (amino acids 276-527 of SEQ ID NO:18).

24. (new) The method according to claim 12, wherein said heterologous protein is the K2S variant of tissue plasminogen activator.

25. (new) The method according to claim 24, wherein said K2S variant is selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14. SEQ ID NO:15, SEQ ID NO:16, and SEQ ID NO: 17.

26. (new) The method according to claim 12, wherein the vector is a phagemid vector comprising DNA coding for OmpA signal peptide (SEQ ID NO:1) and DNA coding for gpIII.

27. (new) The method according to claim 12, wherein the vector comprises the pComb3HSS phagemid.

28. (new) The method according to claim 12, wherein the DNA sequence of OmpA comprises

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCT ACCGTG GCCCAGGCGGCC (SEQ ID NO:1).

29. (new) The method according to claim 12, wherein the DNA sequence of OmpA consists of

ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCT ACCGTG GCCCAGGCGGCC (SEQ ID NO:1).

30. (new) The method according to claim 12, wherein the DNA of the heterologous protein is preceeded by a lac promotor and/or a ribosomal binding site.

31. (new) A method for the production of recombinant tissue plasminogen activator in prokaryotic cells comprising:

expressing a vector in said prokaryotic cells which comprises DNA encoding said tissue plasminogen activator operably linked to DNA encoding the OmpA signal peptide (SEQ ID NO:1);

wherein said tissue plasminogen activator (tPA) is secreted extracellularly as an active protein.

32. (new) The method according to claim 31, wherein said tissue plasminogen activator is secreted as a correctly folded protein.

33. (new) The method according to claim 31, wherein the recombinant tissue plasminogen activator is human tissue plasminogen activator.

34. (new) The method according to claim 31, wherein said DNA sequence encoding said OmpA signal peptide is operatively linked to a nucleic acid sequence encoding a peptide selected from the group consisting of SEGN (SEQ ID NO:2) and SEGNSD (SEQ ID NO:3).

35. (new) The method according to claim 34, wherein said nucleic acid sequence encodes the peptide SEGN (SEQ ID NO:2).

36. (new) The method according to claim 35, wherein said nucleic acid sequence comprises TCTGAGGGAAAC (SEQ ID NO:4).

37. (new) The method according to claim 34, wherein said nucleic acid sequence encodes the peptide SEGNSD (SEQ ID NO:3).

38. (new) The method according to claim 37, wherein said nucleic acid sequence comprises TCTGAGGGAAACAGTGAC (SEQ ID NO:5).

39. (new) The method according to claim 31, wherein the prokaryotic cell is *E. coli*.

40. (new) A method for the production of recombinant tissue plasminogen activator in prokaryotic cells comprising:

a) amplifying DNA encoding said tissue plasminogen activator by PCR;

b) purifying the PCR product;

c) inserting said PCR product into a vector,

wherein said vector comprises a DNA encoding an OmpA signal peptide and DNA encoding gpIII; and

wherein said PCR product is operably linked downstream to the DNA encoding the OmpA signal peptide and operably linked upstream to the DNA encoding gpIII of said vector;

d) inserting a stop codon between the heterologous protein and gpIII; and

e) expressing said vector in the prokaryotic cell.

41. (new) The method according to claim 40, further comprising:

f) purifying said heterologous protein.

42. (new) The method according to claim 40, wherein the tissue plasminogen activator is human tissue plasminogen activator.

43. (new) The method according to claim 40, wherein the vector further comprises a DNA encoding a peptide selected from the group consisting of SEGN (SEQ ID NO: 2) and SEGNSD (SEQ ID NO:3).

44. (new) The method according to claim 31, wherein the tissue plasminogen activator is a fragment or variant thereof.

45. (new) The method according to claim 44, wherein said fragment is selected from the group consisting of:

a) Finger domain (amino acids 4-50 of SEQ ID NO:18);

b) Growth factor domain (amino acids 50-87 of SEQ ID NO:18);

c) Kringle domain 1 (amino acids 86-176 of SEQ ID NO:18);

d) Kringle domain 2 (amino acids 176-262 of SEQ ID NO:18); and

e) Protease domain (amino acids 276-527 of SEQ ID NO:18).

46. (new) The method according to claim 44, wherein said variant is the K2S variant of tissue plasminogen activator.

47. (new) The method according to claim 46, wherein said K2S variant is selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14. SEQ ID NO:15, SEQ ID NO:16, and SEQ ID NO: 17.

48. (new) The method according to claim 31, wherein the vector is a phagemid vector comprising DNA coding for OmpA signal peptide (SEQ ID NO:1) and DNA coding for gpIII.

49. (new) The method according to claim 48, wherein the phagemid vector further comprises DNA coding for the peptide SEGN (SEQ ID NO: 2) or the peptide

SEGNSD (SEQ ID NO:3).

50. (new) The method according to claim 31, wherein the vector comprises the pComb3HSS phagemid.

51. (new) The method according to claim 31, wherein the DNA sequence of OmpA comprises ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCT ACCGTG GCCCAGGCGGCC (SEQ ID NO:1).

52. (new) The method according to claim 31, wherein the DNA sequence of OmpA consists of ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCT ACCGTG GCCCAGGCGGCC (SEQ ID NO:1).

53. (new) The method according to claim 31, wherein the DNA of the heterologous protein is preceeded by a lac promotor and/or a ribosomal binding site.

Remarks

Upon entry of the foregoing amendment, claims 12-53 are pending in the application, with claims 12, 19, 31 and 40 being the independent claims. Claims 1-11 have been cancelled without prejudice to or disclaimer of the subject matter therein. New claims 12-53 have been added. Support for new claims 12-13, 19-20, 31-32 and 40-41, can be found, inter alia, in the specification at paragraphs [0036], [0038], [0039] and in originally filed claim 1. Support for new claims 14-15 and 35-36 can be found, inter alia, in the specification at paragraph [0038]. Support for new claims 16-17 and 37-38 can be found, inter alia, in the specification at paragraph [0039] and original claim 2. Support for new